Remarks

Claims 25-50, 60-131 and 133-155 will be pending in this application upon entry of the present amendment.

Claim 132 has been cancelled without prejudice or disclaimer. Claims 26, 41, 116, 140 and 151 have been amended. Applicants expressly assert that the claims were cancelled or amended for the sole purpose of facilitating prosecution or to more clearly define the invention claimed by the Applicant, and not in an effort to overcome the 35 U.S.C. §102 rejections based on cited prior art, nor in an effort to overcome rejections based on 35 U.S.C. § 112. The new claims 152-155 are fully supported by the specification as originally filed, and lie within the scope of claims already in prosecution. Support for newly added claims 152-155 can be found in the originally filed specification at, for example, page 8, first full paragraph, page 23, first full paragraph, and page 56, first full paragraph.

Thus, no new matter has been added by way of amendments to the specification or the claims.

I. Rejections Under 35 U.S.C. §101

The Examiner rejects claims 25-50 and 60-151 under 35 U.S.C. § 101 because the claimed invention allegedly is not supported by either a specific, substantial and credible asserted utility or a well-established utility, as set forth in item 9 of Paper 11.

More specifically, the Examiner contends:

> [T]he specification has not put forth which, if any, of the multitude of cytokines the instant polypeptide is a receptor of. Therefore, one of skill in the art would have to perform further research and investigation in order to find out, which, if any, cytokine the instant polypeptides could be used with. Applicant argues that the specification states that the instant polypeptides could be used to activate the Jak/stat pathway, however, the locations in the specification pointed to by Applicant are only invitations to the skilled artisan to begin further research and investigation to try and find some connection between the instant polypeptides and any *particular* relationship with any *particular* Jak/stat pathway. The specification merely recites general properties of known cytokine receptor family members and merely asserts that the instant polypeptides may be useful in "treating deficiencies or disorders of the immune system, by activating or inhibiting the proliferation, differentiation, mobilization of immune cells (see page 56, lines 1-5) but does provide any specific details as to which of these properties

> could actually be affected by using the instant polypeptides in any particular way.

(*See,* Paper No. 15, Pages 3-4, Paragraph 6.)

Applicants respectfully disagree and traverse.

A rejection under 35 U.S.C. § 101 is improper when a person of ordinary skill in the art would find credible disclosed features or characteristics of the invention, or statements made by the Applicant in the written description of the invention. *See* M.P.E.P. §§ 2107.01(II), (III) at 2100-[29-31] (Rev. 1, Feb. 2000). In addition, an Applicant need only make *one* credible assertion of utility for the claimed invention to satisfy 35 U.S.C. § 101 and 35 U.S.C. §112; additional statements of utility, even if not "credible," do not render the claimed invention lacking in utility. *See, e.g., Raytheon v. Roper,* 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983), *cert. denied,* 469 U.S. 835 (1984) ("When a properly claimed invention meets at least one stated objective, utility under 35 U.S.C. § 101 is clearly shown."). *See,* M.P.E.P. at 2100-29. Finding a lack of utility is also improper if a person of ordinary skill in the art would know of a use for the claimed invention at the time the application was filed. M.P.E.P. § 2107.01(II)(B) at 2100-[29-30].

Further, the Federal Circuit has recently stated with respect to the rejection of claims for lack of utility that:

> The PTO cannot make this type of rejection...unless it has reason to doubt the objective truth of the statements contained in the written description. *See Brana,* 51 F.3d at 1566, 34 USPQ2d at 1441 ("[T]he PTO has the initial burden of challenging a presumptively correct assertion of utility in the disclosure. Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility.")(citations omitted); *In re Marzocchi,* 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971)....The PTO may establish a reason to doubt an invention's asserted utility when the written description "suggest[s] an inherently unbelievable undertaking or involve[s] implausible scientific principles." *Brana,* 51 F.3d at 1566, 34 USPQ2d at 1441; see also *In re Eltgroth,* 419 F.2d 918, 164 USPQ 221 (CCPA 1970) (control of aging process).

In re Cortright, 49 U.S.P.Q.2d 1464, 1466 (Fed. Cir. 1999). Thus, the initial burden is on the Examiner to establish why one of ordinary skill in the art would *reasonably doubt* Applicants' assertions regarding utility. However, the Examiner has not met the necessary burden to establish and maintain a rejection of the claims for lack of utility under 35 U.S.C. §101.

Contrary to the Examiner's comments, Applicants have set forth in the specification statements that clearly and fully describe the function of CRCGCL and explain why Applicants believe the invention is useful. For example, the specification explicitly teaches that the clone containing the cDNA encoding CRCGCL was isolated from an activated T-cell cDNA library (*see, e.g.,* the specification at page 7, line 1). Further the specification discloses:

> Subsequent Northern analysis also showed a 1.6 Kb transcript in a cervical cancer cell line (HeLa), activated T cells, and a lung carcinoma cell line (A549), while a shorter variant is also expressed in the lymph node and to a lesser extent in the spleen tissues, a pattern consistent with immune specific expression.
>
> CRCGCL expression was not observed in the following cell lines, HL60, K562, Molt-4, Raji, SW480, G361, as well as the heart, brain, placenta, lung, liver, skeletal muscle, kidney, pancreas, thymus, prostate, testis, ovary, small intestine, colon, or peripheral blood leukocytes, a pattern consistent with immune specific expression.

(See, e.g., the specification at page 7, lines 15-23.) In addition, the specification, at the bottom of page 7, line 35, through the top of page 8, line 2, states that "[b]ecause Interleukin-2 receptor gamma (Accession Nos. 1532088) is thought to be important as a cytokine receptor, the homology between Interleukin-2 receptor gamma (Accession No. 1532088) and CRCGCL suggests that CRCGCL may also be involved in the differentiation and proliferation of cells."

As noted in the specification at page 7, lines 24-34 and Figure 2, the CRCGCL protein is homologous to the Interleukin-2 receptor (IL-2R) gamma chain. Applicants respectfully point out that the role of IL-2R gamma chain, and the cytokine that binds it, IL-2, were well-established in the art at the priority date of the invention. IL-2 is a cytokine that plays a pivotal role in the regulation of T cell-mediated immune responses (*see, e.g.,* Lin et al., J. Biol. Chem 271:10738-10744 (1996); and Taniguchi, T., Science 268:251-255 (1995)). It was known that mutations in the IL-2R gamma chain lead to X-linked severe combined immunodeficiency (XSCID) in humans and several lymphocyte abnormalities in mice (*see, e.g.,* Leonard et al., Immunol. Rev. 148:97-114 (1995); and Noguchi, M. Cell 73:147-157 (1993)).

As a result, at page 45, line 19, Applicants specifically assert that "CRCGCL polypeptides can be used to treat disease." One of skill in the art would clearly recognize, and as it is explicitly stated in the specification, CRCGCL polypeptides would encompass soluble forms of CRCGCL which could reduce the activity of the membrane bound receptor by

competing with it for free ligand (*see, e.g.,* the specification at page 45, lines 24-26, and as quoted below). In addition, at page 45, lines 28-29, Applicants teach that "antibodies directed to CRCGCL polypeptides can also be used to treat disease." Further, at page 56, lines 3-5, the specification explicitly states: "CRCGCL polypeptides or polynucleotides may be useful in treating deficiencies or disorders of the immune system, by activating or inhibiting the proliferation, differentiation, or mobilization (chemotaxis) of immune cells."

Applicants have also specifically contemplated agonists and antagonists of CRCGCL, including, but not limited to, for example, antibodies directed against CRCGCL, soluble fragments of CRCGCL, antisense molecules, and ribozymes, (*see, e.g.,* the specification at page 31, line 17 through page 32, line 5; page 45, lines 20-32; page 62, lines 4-7 and line 36 through page 63, line 2; page 63, line 14 through page 67, line 14; page 80, lines 17-18). For example, Applicants explicitly teach, at page 57, lines 5-8, that "the administration of CRCGCL polypeptides or polynucleotides that can inhibit an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing autoimmune disorders." For example, the skilled artisan would readily recognize, and as explicitly stated in the specification, that a soluble fragment of CRCGCL could be used to inhibit the proliferation, differentiation, or chemotaxis of T-cells, and thus be effective therapy in preventing autoimmune disorders. As stated in the specification at page 45, lines 20-26:

> [P]atients can be administered CRCGCL polypeptides in an effort. . . to reduce the activity of a membrane bound receptor by competing with it for free ligand (*e.g.,* soluble TNF receptors used in reducing inflammation). . .

Further, Applicants have asserted T-cell related diseases and disorders that can be treated by CRCGCL polypeptides and antagonists thereof:

> The tissue distribution of this gene in cells of the immune system suggests that the protein product of this clone would be useful for treatment, prophylaxis and diagnosis of immune and autoimmune diseases, such as lupus, transplant rejection, allergic reactions, arthritis, asthma, immunodeficiency diseases, leukemia, AIDS. In addition, its expression in T-cells suggests a potential role in the treatment, prophylaxis and detection of thymus disorders such as Graves Disease, lymphocytic thyroiditis, hyperthyroidism and hypothyroidism. The receptor could also serve as a target for small molecule or monoclonal antibody, blocking its activity, which could be important in the disease states listed herein.

(*See, e.g.,* the specification at page 8, line 32, through page 9, line 6.)

Thus, Applicants have asserted specific, substantial and credible utilities for CRCGCL, for example, to generate antagonists (including, but not limited to, for example, antibodies against CRCGCL; and/or soluble fragments of CRCGCL) which would be useful in inhibiting the proliferation, differentiation or chemotaxis of T-cells, and in the treatment of T-cell related disorders, including autoimmune disorders, such as leukemia.

CRCGCL has become known in the art as "TSLPR" and has been shown to be a receptor for thymic stromal lymphopoietin (TSLP), a cytokine now known in the art. It is now known that TSLP binds a complex comprising both CRCGCL and the IL-7 receptor (IL-7R) alpha chain. *See,* for example: Reche et al. (J. Immunol. 167:336-343 (2001)), and Quentmeier et al. (Leukemia 15:1286-92 (2001), submitted herewith as Exhibits A and B, respectively).

Further, in corroboration of Applicants asserted utilities[1], Applicants respectfully direct the attention of the Examiner to publications wherein CRCGCL has been reported to be correlated with costimulation of thymocytes and mature T cells and T-cell chemotaxis as disclosed in the specification (*see, e.g.,* the specification at page 56, lines 3-5) and wherein CRCGCL antagonists are reported to be useful to inhibit T-cell chemotaxis and stimulation of thymocytes and mature T cells as asserted in the specification (*see, e.g.,* the specification at page 57, lines 5-8). For example, Reche et al. demonstrate that CRCGCL (TSLPR) is expressed primarily in dendritic cells, monocytes and T-cells (*see, e.g.,* Reche et al., *supra*, at page 339, second column and Figure 4). In addition, Reche et al. show that TSLP can induce the release of T cell-attracting chemokines from monocytes and potently enhance the T cell stimulatory capacity of the CD11c+ subset of dendritic cells (*see, e.g.,* Reche et al., *supra*, at page 336, pages 339 and 340, and Figures 5 and 6). Further, Reche et al., assert that a soluble form of CRCGCL (TSLPR) could serve as an inhibitor of TSLP, and thus an inhibitor of the release of T cell-attracting chemokines from monocytes and the enhancement of the T cell stimulatory capacity of the CD11c+ subset of dendritic cells (*see, e.g.,* Reche et al., *supra*, at

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[1] Applicants point out that the Reche et al. and Quentmeier et al. references are being used to demonstrate the credibility of Applicants' asserted utility. Legal precedent for the use of post-filing date references in this manner can be found in *In re Brana*, where the courts stated:

> The Kluge declaration, though dated after applicants' filing date, can be used to substantiate any doubts as to the asserted utility since this pertains to the accuracy of a statement already in the specification. *In re Marzocchi, 439 F.2d at 224 n.4, 169 U.S.P.Q. (BNA) at 370 n.4.*

(*See, In re Brana, 51 F.3d 1560 at 1567 n.19, 34 U.S.P.Q.2D (BNA) 1436 (March 30, 1995).)*

page 338, second column).

Moreover, Quentmeier et al. have demonstrated that TSLP induces the growth and prevents the apoptosis of the acute myeloid leukemia (AML)-derived cell line MUTZ-3 (*see, e.g.,* Quentmeier et al., *supra*, at page 1289, and Figures 4-6). The complex that binds TSLP is known to comprise IL7R and CRCGCL. Quentmeier et al. show that a monoclonal antibody directed against the IL-7R alpha chain can effectively neutralize the TSLP-induced proliferation of MUTZ-3 cells (*see, e.g.,* Quentmeier et al., *supra*, at page 1290, and Figure 7). These results show that antagonists of TSLP can inhibit the proliferation of leukemia cells, and thus would be useful in treating leukemia. Therefore, one of ordinary skill in the art would readily conclude that antagonists of CRCGCL would have a similar effect. In addition, Applicants have contemplated and disclosed the therapeutic use of soluble fragments of CRCGCL to treat disease, such as, for example, leukemia, by inhibiting the action of CRCGCL or by binding to its ligand (*see, e.g.,* specification at page 8, line 34 through page 9, line 1; page 45, lines 24-25; page 62, lines 3-14 and line 37 through page 63, line 2). Applicants have furthermore confirmed by experimental evidence provided in their Declaration submitted with Paper 14, that the soluble extracellular form of CRCGCL can bind TSLP and inhibit the activity of CRCGCL, thus showing the antagonist activity.

Thus, the published literature cited above demonstrates that antagonists of CRCGCL can inhibit the proliferation, differentiation or chemotaxis of T-cells and that this activity is reasonably correlated with, for example, the asserted use in the treatment of autoimmune disorders, such as leukemia, disclosed in the specification at page 8, line 32, through page 9, line 6. *In re Brana, 51 F.3d 1560, 34 USQP2d 1436 (Fed. Cir. 1995); Cross v. Izuka 753 F.2d 1040 (Fed. Cir. 1985).* Therefore, the documentary evidence cited above confirms the credibility, as well as the specificity and substantiality, of the asserted utility for CRCGCL. Thus, the claimed compositions and methods are useful, as asserted in the specification, under § 101.

Applicants have disclosed a specific, substantial and credible utility of CRCGCL, for example, to generate antagonists (including, but not limited to, for example, antibodies against CRCGCL; and/or soluble fragments of CRCGCL) which would be useful in inhibiting the proliferation, differentiation or chemotaxis of T-cells, and in the treatment of T-cell related disorders including autoimmune disorders, such as leukemia. Applicants have provided post filing date evidence from Reche et al., and Quentmeier et al. in addition to the evidence provided in the Declaration of Paul Moore submitted with Paper No. 14, which

demonstrates that the asserted utilities would be found by one of ordinary skill in the art to be more likely than not true.

Thus, the above asserted utilities for CRCGCL are specific (the vast majority of proteins cannot be used to generate antagonists (including, but not limited to, for example, antibodies against CRCGCL; and/or soluble fragments of CRCGCL) which would be useful in inhibiting the proliferation, differentiation or chemotaxis of T-cells, and in the treatment of autoimmune disorders, such as leukemia) and substantial ("the general rule [is] that the treatments of specific diseases or conditions meet the criteria of 35 U.S.C. § 101." (Revised Interim Utility Guidelines Training Materials, p. 6)). In addition, the evidence of record demonstrates that they are credible to one of ordinary skill in the art.

With regard to these asserted therapeutic activities, Applicants note that there is no need to prove that a correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty or provide actual evidence of success in treating humans where such a utility is asserted. M.P.E.P. § 2107.02 (I) at 2100-[33-34]. All that is required of Applicants is that there be a reasonable correlation between the biological activity and the asserted utility. *See, Nelson v. Bowler*, 626 F.2d 853, 857 (C.C.P.A. 1980). Moreover, "[u]sefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans." *In re Brana*, *51* F.3d *1560*, *1568* (Fed. Cir. 1995) (emphasis added).

Even assuming, *arguendo*, the Examiner has established a *prima facie* showing that the claimed invention lacks utility, Applicants respectfully submit that they have rebutted the Examiner's showing by proffering sufficient evidence to lead one skilled in the art to conclude that the asserted utilities are more likely than not true. Applicants have directed the Examiner to the specification where clear and specific assertions are made of CRCGCL biological and therapeutic activity and provided experimental evidence confirming the asserted utilities.

In view of the above, Applicants submit that the asserted utilities of the invention meet the statutory requirement set forth in 35 U.S.C. § 101. The Examiner has failed to establish and maintain grounds as to why a rejection for lack of utility is proper. Accordingly, Applicants respectfully request that the rejection be withdrawn.

II. Rejections Under 35 U.S.C. §112, First Paragraph

A. The Examiner further rejects claims 25-50 and 60-151 under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement.

More specifically, the Examiner contends that "since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation." (*See,* Paper No. 15, Page 5, Paragraph 7.)

Applicants respectfully disagree and traverse.

For the reasons discussed above in response to the rejection under 35 U.S.C. § 101, Applicants submit that the claimed invention is supported by a specific and substantial or well-established utility. The Examiner "should not impose a 35 U.S.C. § 112, first paragraph, rejection grounded on a "lack of utility" basis unless a 35 U.S.C. § 101 rejection is proper." M.P.E.P. § 2107(IV) at 2100-28 (Rev.1, Feb. 2000). Therefore, since the claimed invention complies with the utility requirement of 35 U.S.C. § 101, the rejection of claims under 35 U.S.C. § 112, first paragraph, based on lack of utility of the claimed invention, should be withdrawn.

B. The Examiner further rejects claims 25-50 and 60-151 under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement in their full scope.

More particularly, the Examiner alleges:

> [T]he issue is not that sequence variants could be created, but that the specification has not taught which variants, of the almost infinite number of variants that could be created, could be made that preserve and/or create any desired functional property of the polypeptide. Nor has the specification taught how to use any of the claimed polynucleotides that encode variants but which do not have any asserted functional properties. While it may be true that functional variants typically contain only conservative variation or variation in non-critical residues or non-critical regions, this teaching does not provide any information as to where these sites of conservative variation, non-critical residues, or non-critical regions could be – such information being necessary to enable the skilled artisan to make and use the claimed invention without undue experimentation. Further the specification failed to provide guidance as to what any particular functional property of the claimed polypeptide is; nor any particular functional difference between the polypeptide and sequence variants of the polypeptide. Thus, one of skill in the art

would not know how to create a variant of a polypeptide having a particular function if that function was not known.

(*See,* Paper No. 15, Page 7, Paragraph 7.)

Applicants respectfully disagree and traverse.

Preliminarily, Applicants point out that in order to enable the claimed invention as required by 35 U.S.C. § 112, the specification need only enable a person of ordinary skill in the art to make the polypeptides encoded by the claimed polynucleotides and practice a single use thereof without undue experimentation.[2] Thus, Applicants submit that to be fully enabled, the polypeptides of the invention encoded by the claimed polynucleotides need merely have application in a single use, such as, for example, to generate antibodies that immunospecifically bind the polypeptides of the invention which would be useful in detecting or purifying CRCGCL; to generate antagonists (including, but not limited to, for example, antibodies against CRCGCL; and/or soluble fragments of CRCGCL) which would be useful in inhibiting the proliferation, differentiation or chemotaxis of T-cells, and in the treatment of autoimmune disorders, such as leukemia. Because the CRCGCL polypeptides of the invention have a credible, specific and substantial use, antagonists of CRCGCL also have utility (including, but not limited to, for example, antibodies against CRCGCL; and/or soluble fragments of CRCGCL).

Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. *Fields v. Conover*, 170 USPQ 276, 279 (C.C.P.A. 1971). The factors that can be considered in determining whether an amount of experimentation is undue have been listed in *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Among these factors are: the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of pertinent literature and the level of skill in the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine. Id.

While the predictability of the art can be considered in determining whether an amount of experimentation is undue, mere unpredictability of the result of the experiment is not a consideration. Indeed, the Court of Custom and Patent Appeals has specifically

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[2] The Applicant need show utility for only one disclosed purpose. See *Raytheon Co. v. Roper Corp.*, 220 USPQ 592 (Fed. Cir. 1983, *cert. denied*, 469 U.S. 835 (1984); *Ex parte Lanham*, 121 USPQ 223 (Pat. Off. Bd. App. 1958).

cautioned that the unpredictability of the result of an experiment is not a basis to conclude that the amount of experimentation is undue in *In re Angstadt*, 190 USPQ 214 (C.C.P.A. 1976):

> [If to fulfill the requirements of 112, first paragraph, an applicant's] disclosure must provide guidance which will enable one skilled in the art to determine, with reasonable certainty before performing the reaction whether the claimed product will be obtained, . . . then all "experimentation" is "undue" since the term "experimentation" implies that the success of the particular activity is uncertain. Such a proposition is contrary to the basic policy of the Patent Act.

Id. at 219 (emphasis in the original). As in all cases, this is the test: whether it would require undue experimentation to practice the invention – even when a claim might encompass some inoperative embodiments. As the Federal Circuit states:

> It is not a function of the claims to specifically exclude. . . possible inoperative stubstances. . . Of course, if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid.

Atlas Powder v. E.I. Du Pont de Nemours & Co. 750 F.2d 1569, 224 U.S.P.Q. (BNA) 409 (Fed. Cir. 1984).

Since the disclosed or otherwise known methods of making and screening polypeptides (and fragments or variants thereof) encoded by the claimed polynucleotides may be used to make and then determine, without undue experimentation, whether a given polypeptide encoded by a polynucleotide encompassed by the claims is able to, for example, generate an immunospecific antibody which would be useful in detecting or purifying CRCGCK; generate antagonists (including, but not limited to, for example, antibodies against CRCGCL; and/or soluble fragments of CRCGCL) which would be useful in inhibiting the proliferation, differentiation or chemotaxis of T-cells, and in the treatment of autoimmune disorders, such as leukemia and therefore possesses the disclosed utility, the enablement requirement is fully satisfied. *In re Wands*, 8 USPQ2d at 1404; *Ex parte Mark*, 12 USPQ2d 1904, 1906-1907 (B.P.A.I. 1989).

The specification provides ample guidance for one of ordinary skill in the art to routinely make and use the polypeptides encoded by the claimed polynucleotides of the present invention. The specification discloses routine methods for generating antibodies directed to CRCGCL (*see, e.g.*, pages 27-32; and Example 11), routine methods to identify antagonists of CRCGCL (*see, e.g.*, pages 62-63), and biological assays including, for

example, assays to determine if a protein proliferates T-cells (*see, e.g.*, pages 88-89, Example 14; and pages 92-94, Example 17), and assays to determine if a protein proliferates or differentiates myeloid cells (*see, e.g.*, page 90, Example 15). Antibodies generated according to methods disclosed in the specification or otherwise known in the art may routinely be applied to determine whether these antibodies immunospecifically bind the polypeptides encoded by the claimed polynucleotides.

Applicants submit that because of (1) the disclosure and characterization in the specification of the nucleic acid and polypeptide sequence corresponding to CRCGCL; (2) the availability of routine techniques for generating fragments or variants to a known nucleic acid sequence, for expressing the polypeptide encoded by the fragments or variants, for generating antibodies against the polypeptide, for assaying the ability of a nucleic acid to function as a probe, for assaying the ability of an antibody to immunospecifically bind a polypeptide; for assaying the ability of a polypeptide or antibody to inhibit the proliferation, differentiation and/or chemotaxis of T cells; (3) the high level of skill in the field of molecular biology and immunology; and (4) the direction and guidance provided by the specification, one skilled in the art could routinely generate the claimed nucleic acids and determine whether these nucleic acids encode polypeptides that bind an antibody that immunospecifically bind CRCGCL; or whether these nucleic acids encode polypeptides that inhibit T cell proliferation, differentiation, and/or chemotaxis; or whether antibodies generated against polypeptides encoded by these nucleic acids inhibit T cell proliferation differentiation and/or chemotaxis.

A patent specification which teaches how to make and use the invention must be taken as enabling unless the Patent Office provides sufficient reason to doubt the accuracy of the disclosure. *In re Marzocchi*, 439 F.2d. 220, 223-224, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971). Applicants submit that the Examiner has provided no evidence to doubt the enablement of the claimed CRCGCL polynucleotides to, for example, generate an immunospecific antibody, or generate antagonists (including, but not limited to, antibodies against CRCGCL and/or soluble fragments of CRCGCL).

In view of the foregoing, Applicants submit that the claims fully meet the enablement requirements of Section 112, first paragraph, and respectfully request that the rejection be withdrawn.

New Rejections:

III. Rejections Under 35 U.S.C. §112, Second Paragraph

A. The Examiner rejects claims 33, 50, 107, 123, 131, 139, and 150 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

More specifically, the Examiner contends:

> The claims 33, 50, 107, 123, 131, 139, and 150 require a composition. A composition necessarily requires more than one component, yet the claims do not recite such a component. Therefore the metes and bounds of the claims cannot be determined. If Applicant deems it proper, one way to obviate this rejection is amend the claims to recite a composition comprising the polynucleotide and a carrier.

(*See,* Paper No. 15, Page 8, Paragraph 9.)

This rejection has been rendered moot by the Examiner's statement in the Interview Summary of November 8, 2001.

B. The Examiner further rejects claim 140 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. More specifically, the Examiner contends that "[i]t is unclear what the word "modulate" is intended to encompass, e.g., enhancement, inhibition, or some other feature. . . . [t]herefore, the metes and bounds of the claim cannot be determined." (*See*, Paper No. 15, Page 8, Paragraph 9.)

Although Applicants disagree that the claim as written is indefinite, Applicants have amended claim 140, and added new claims 152-153. As one of skill in the art would recognize, the use of the word "modulates" in the art is well understood and routinely used to encompass the terms "inhibits" and "enhances." Applicants have amended the claim to avoid the use of the word "modulate" which the Examiner finds offensive. Applicants note that their amendment to the claims in no way narrows the scope as the terms used are equivalents. Although the Examiner did not reject claim 151, in an effort to facilitate prosecution, Applicants have amended claim 151 in a similar manner, and added claims 154-155. New claims 152-155 which find support in the originally filed specification at, for example, page 8, first full paragraph, page 23, first full paragraph, and page 56, first full paragraph.

Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

IV. Rejections Under 35 U.S.C. §112, First Paragraph

A. The Examiner rejects claims 25-50 and 60-151 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

More particularly, the Examiner alleges that:

> The specification discloses a polynucleotide of SEQ ID NO:1, yet the claims encompass polynucleotides not described in the specification, e.g., sequences from other species, mutated sequences, allelic variants, or sequences that have a recited degree of identity. None of these sequences meet the written description provision of 35 U.S.C. §112, first paragraph. Although one of skill in the art would reasonably predict that these sequences exist, one would not be able to make useful predictions as to the nucleotide positions or identities of those sequences based on the information disclosed in the specification.
>
> With the exception of the polynucleotide of SEQ ID NO:1, the skilled artisan cannot envision the detailed chemical structure of the encompassed variants. Therefore, only the polynucleotide of SEQ ID NO:1, and polynucleotides *consisting* of fragments thereof, but not the full breadth of the claims meet the written description provisions of 35 U.S.C. §112, first paragraph.

(*See*, Paper No. 15, Page 9, Paragraph 11.)

Applicants respectfully disagree and traverse.

The test for the written description requirement is whether one of ordinary skill in the art could reasonably conclude that the inventor has possession of the claimed invention in the specification as filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991); M.P.E.P. § 2163.02. Further, the Federal Circuit recently re-emphasized the well-settled principle of law that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [they] invented what is claimed,'" *Union Oil Co. v. Atlantic Richfield Co.*, 208 F.3d 989, 54 U.S.P.Q.2d 1227 (Fed. Cir. 2000). The court emphasized the importance of what the person of ordinary skill in the art would understand from reading the specification, rather than whether the specific embodiments had been explicitly described or exemplified. Indeed, as

the court noted, "the issue is whether one of skill in the art could derive the claimed ranges from the patent's disclosure." *Unocal*, 208 F.3d at 1001 (emphasis added).

In an analysis of written description under 35 U.S.C. § 112, first paragraph, the Examiner bears the initial burden of presenting a *prima facie* case of unpatentability. This burden is only discharged if the Examiner can present evidence or reasons why one of ordinary skill in the art would not reasonably conclude that Applicants possessed the subject matter as of the priority date of the present application. *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ2d 90, 96 (C.C.P.A. 1976); M.P.E.P. § 2163.04. In the instant case, the Examiner has not met this burden.

The Examiner contends that "one would not be able to make *useful* predictions as to the nucleotide positions or identities of those sequences based on the information disclosed in the specification" (*see,* Paper No. 15, Page 9, Paragraph 11, emphasis added). Applicants note that the Examiner appears to be arguing that some characteristic (*e.g.*, usefulness) of the claimed polynucleotides beyond the sequence disclosed in the specification is required to satisfy the written description requirement. Applicants respectfully disagree with the Examiner and point out that the written description requirement "is separate and distinct from the enablement requirement" (*see,* M.P.E.P. § 2163 I. August 2001 Revision at page 2100-155, citing *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1560 (Fed Cir. 1991)). Applicants note that the proper legal standard upon which to judge written description is not "useful predictions" but rather whether the claimed invention could be derived by one of skill in the art, as discussed above.

Accordingly, one skilled in the art would reasonably conclude that Applicants had possession of the polynucleotides encompassed by the rejected claims in the present application as filed. Furthermore, Applicants respectfully note that the Examiner has underestimated both the teaching of the present application and the level of skill in the art on the priority date of the present application.

Applicants have provided the skilled artisan with the DNA (SEQ ID NO:1) and polypeptide (SEQ ID NO:2) sequences of CRCGCL. Applicants have also deposited a cDNA clone encoding the polypeptide of the present invention with the American Type Culture Collection pursuant to the Budapest Treaty (ATCC No. 209691, deposited March 23, 1998, and 209641, deposited February 25, 1998). Thus, the present specification does in fact, describe the core structural feature common to all of the polypeptides encoded by the claimed polynucleotides (*e.g.*, SEQ ID NO:2 or the protein encoded by the cDNA contained in the

ATCC Deposit). Further, Applicants have also described variants of CRCGCL, including specific degrees of homology and number of substitutions in the amino acid sequence of CRCGCL that are specifically contemplated, and the polynucleotides encoding them. Accordingly, one skilled in the art, enlightened by the teachings of the present application, could quite readily recognize the polypeptides encoded by the claimed polynucleotides, as distinguished from those not claimed (*i.e.,* polypeptides having less than 95% amino acid sequence identity to or greater than 30 amino acid substitutions in SEQ ID NO:2 or the protein encoded by the cDNA contained in the ATCC Deposit).

It is also well established that "[a} gene is a chemical compound, albeit a complex one". *Amgen, Inc. v. Chugai Pharmaceutical Co., LTD.,* 927 F.2d 1200, 1206 (Fed. Cir. 1991). And, claims of the instant application, directed to polynucleotides encoding polypeptides having 95% or more identity with SEQ ID NO:2 or the protein encoded by the cDNA in ATCC Deposit No. 209691 or 209641, and to polynucleotides encoding polypeptides having one to thirty amino acid substitutions in SEQ ID NO:2 or the protein encoded by the cDNA in ATCC Deposit No. 209691 or 209641, are essentially the same as to chemical claims involving generic chemical formulas. As stated by Judge Lourie in *University of California v. Eli Lilly*, "In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass." All of the objectives met by a generic chemical formula are similarly met by the explicit description of a DNA and polypeptide sequence (i.e., SEQ ID NOS:1 and 2) and the claims to polynucleotides encoding polypeptides having 95% or more identity with that sequence and/or polypeptides having one to thirty amino acid substitutions in that sequence. That is, the claims to the present invention clearly distinguish the boundaries of the claimed genus and identify all of the members of that genus. Any skilled artisan can readily identify every polynucleotide encoding a polypeptide having the recited % identity of SEQ ID NO:2 or of the protein encoded by the cDNA contained in the Deposit, or having the recited number of amino acid substitutions in the sequence of SEQ ID NO:2 or of the protein encoded by the cDNA contained in the Deposit, and distinguish them from other materials. Accordingly, one skilled in the art would reasonably conclude that Applicants had possession of the polynucleotides encompassed by the rejected claims (and the encoded polypeptides), upon reading the application as filed.

For all of the above reasons, Applicants respectfully emphasize that the Examiner has failed to meet the required burden in presenting evidence or reasons why those skilled in the art would not recognize the claimed invention from the disclosure. Moreover, the specification conveys with reasonable clarity that Applicants were in possession of the claimed invention. Accordingly, Applicants respectfully request that the rejection of claims 111-126 under 35 U.S.C. § 112, first paragraph for inadequate description, be reconsidered and withdrawn.

IV. Rejections Under 35 U.S.C. §102

A. The Examiner rejects claims 26, 42, 116, 124, 132, and 143 under 35 U.S.C. §102(b) as allegedly being anticipated by GenEmbl accession number X91553.

More particularly, the Examiner contends:

> Claims 26, 42, 116, 124, 132, and 143 require polynucleotides that are complementary to a polynucleotide of SEQ ID NO:1 or complementary to polynucleotides of SEQ ID NO:1 are not GenEmbl accession number X91553. GenEmbl accession number X91553 discloses a polynucleotide that is 100% identical to SEQ ID NO:1 over the range of positions 778-806 and would therefore encode a polypeptide having a sequence identical to positions 256-264 of SEQ ID NO:2, and would also be considered to be complementary to both a polynucleotide of SEQ ID NO:1 and to polynucleotides of SEQ ID NO:1 that are not GenEmbl accession number X91553. One of skill in the art appreciates that a polynucleotide can be complementary to another polynucleotide without being complementary over the full length, e.g., a probe. Also, as currently worded, these claims do not exclude X91553.

(*See,* Paper No. 15, Page 10, Paragraph 13.)

Applicants respectfully traverse the rejection under U.S.C. § 102(b).

Nevertheless, in the interest of facilitating prosecution, Applicants have amended claims 26, 124, and 132 to further indicate that the term "complementary" refers to the full length of the polynucleotide; amended claim 116 to recite "wherein said polynucleotide is not Genbank Accession No. X91553;" and cancelled claim 132, thereby mooting the rejection of these claims.

With regard to the rejection of claim 42, Applicants point out that this claim currently reads: "An isolated polynucleotide comprising a nucleic acid encoding at least 30 contiguous amino acids of SEQ ID NO:2". Genbank Accession No. X91553 does not anticipate this claim, as the Genbank sequence would encode a protein with only 7 amino acids in common

with CRCGCL. However, in an effort to facilitate prosecution, Applicants will assume that the Examiner meant to reject claims 41 and 44, which both encompass complementary polynucleotides. Applicants have similarly amended these claims to recite "complementary over its full length," thereby obviating a potential rejection of these claims.

The Examiner further rejects claim 140 under 35 U.S.C. §102(b), as allegedly being anticipated by GenEmbl accession number X91553.

More specifically, the Examiner contends:

> [C]laim 140 requires that the claimed polynucleotide encode a fragment of SEQ ID NO:2, wherein said fragment modulates the differentiation and/or proliferation of immune cells. The polypeptide of SEQ ID NO:2 comprises a fragment consisting of the amino acid phenylalanine (at position 260, for example). GenEmbl accession number X91553 discloses a polynucleotide that comprises a nucleic acid sequence that encodes the amino acid phenylalanine (see above). It is inherent feature of phenylalanine that is capable of promoting the proliferation of all animal cells (immune cells included) because it is an essential amino acid, see Lodish eds, Molecular Biology, page 193.

(*See,* Paper No. 15, Pages 10-11, Paragraph 13.)

Applicants respectfully disagree and traverse.

Anticipation can only be established by a single prior art reference which discloses each and every element of the claimed invention. *Scripps Clinic & Research Found. V. Genentech, Inc.* 927 F.2d 1565, 1576, 18 U.S.P.Q.2d 1001, 1010 (Fed. Cir. 1991), *clarified on recons.*, 18 U.S.P.Q.2d 1896 (Fed. Cir. 1991). In the instant case, the Examiner is attempting to establish an inherent anticipation rejection over Genbank Accession No. X91553 since this reference neither expressly teaches nor suggests the claimed invention.

The Examiner has not shown that the fragment encoded by Genbank Accession No. X91553 which shares sequence identity with CRCGCL can "modulate" (e.g., inhibit or enhance, as amended) the proliferation and/or differentiation of immune cells. The sequence available in Genbank Accession No. X91553 was identified by Jackson et al., in a study to identify sequences attaching loops of nuclear and mitochondrial DNA to underlying structures in human cells (see, e.g., Jackson et al., Nuc. Acids Res. 24:1212-1219 (1996), cited through Genbank Accession No. X91553 and attached hereto as Exibit C). Jackson et al. do not describe a polypeptide fragment encoded by Genbank Accession No. X91553 with sequence identity to CRCGCL that modulates (e.g., inhibits or enhances, as amended) the proliferation and/or differentiation of immune cells. Accordingly, Applicants respectfully

submit that under the standard set by the Courts, the sequence available in Genbank Accession No. X91553, does not anticipate the claimed polynucleotides.

Nor can the Examiner establish that the claimed polynucleotides are an inherent characteristic that necessarily flows from the cited Genbank Accession No. X91553, because the prior art product necessarily does not possess the characteristics of the claimed products. MPEP 2112.01 citing *In re Best*, 562 F.2d 1252, 1255 (CCPA 1977) and *Titanium Metals Corp. v. Banner*, 778 F.2d 775 (Fed. Cir. 1985). The Examiner has only alleged that the claimed polynucleotide encoding a polypeptide fragment with modulating activity *may* occur or be present in the prior art, which is not sufficient to establish the inherency of that result or characteristic. MPEP 2112 at 2100-48 citing *In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993) and *In re Oelrich*, 666 F.2d 578, 581-82 (CCPA 1981). Further, the MPEP states:

> In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art.

Id. citing *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original).

The Examiner asserts that because X91553 encodes a 7 amino acid fragment in common with CRCGCL, and this fragment contains a phenylalanine residue, and phenylalanine is an essential amino acid necessary for cell growth, that this fragment anticipates the claimed invention.

Applicants note that as asserted by the Examiner, phenylalanine is an essential amino acid used in cell culture as a nutrient required for cell growth. However, contrary to the Examiner's conclusion that "[i]t is an inherent feature of phenylalanine that it is capable of promoting the proliferation of all animal cells (immune cells included) because it is an essential amino acid," Applicants assert that no reasonable person of skill in the art would equate a protein having "modulating" (e.g., inhibiting or enhancing, as amended) activity with that of an amino acid having nutrient properties. Scientists routinely test proteins for "modulating" (e.g., inhibiting or enhancing, as amended) activity on different cell types, including immune cells. These tests usually require that cells be grown in culture to a certain cell density as a preliminary step in the experiment. The essential amino acids, including phenylalanine, are provided, as nutrients for cell growth. The scientist then add proteins to the cells in culture to test their ability to "modulate" (e.g., inhibit or enhance, as amended) the

proliferation and/or differentiation of the cells in culture, while including a control for the cell proliferation and/or differentiation without the test proteins. One of ordinary skill in the art would clearly recognize the difference between cell proliferation and/or differentiation due to normal media supplied with nutrients and the "modulating" (e.g., inhibiting or enhancing, as amended) effects of a test protein. No reasonable scientist would attribute "modulating" (e.g., inhibiting or enhancing, as amended) activity to an essential nutrient.

Thus, the Genbank Accession No. X91553 disclosure of a polynucleotide encoding a 7 amino acid polypeptide in common with CRCGCL does not anticipate the claimed polynucleotides by inherent anticipation because the elements of Applicants' claims, polynucleotides encoding a fragment of SEQ ID NO:2 or a fragment of a protein encoded by the cDNA contained in ATCC Deposit No. 209691 or 209641, wherein said fragment inhibits or enhances the differentiation and/or proliferation of immune cells (as amended), were neither known, recognized, nor appreciated by anyone at the time of the publication of the reference.

Moreover, because Genbank Accession No. X91553 does not anticipate claim 140, the complement of the sequence available through Genbank Accession No. X91553 would not anticipate claim 143.

In view of the foregoing, Genbank Accession No. X91553 does not anticipate, expressly or inherently, or render obvious the claimed invention. Accordingly, Applicants respectfully request that the rejection of claims 26, 42, 116, 124, 132, 140, and 143 under 35 U.S.C. § 102(e) over Genbank Accession No. X91553 be withdrawn.

Conclusion

In view of the foregoing remarks, applicants believe that this application is now in condition for allowance.

If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Dated: NOVEMBER 21, 2001

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VIA HAND DELIVERY NOVEMBER 21, 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Moore et al.

Attorney Docket No.: PF466

Application Serial No.: 09/263,626

Art Unit: 1646

Filed: March 5, 1999

Examiner: Brannock, M.

For: **Cytokine Receptor Common Gamma Chain Like**

VERSION SHOWING CHANGES MADE

In the Claims:

26. (Once Amended) An isolated [polynucleotide] nucleic acid molecule complementary to the polynucleotide of claim 25, over the full length of said polynucleotide.

41. (Once Amended) An isolated polynucleotide comprising 150 contiguous nucleotides of SEQ ID NO:1 or the full length complement thereof.

44. (Once Amended) An isolated polynucleotide complementary over its full length to the polynucleotide of claim 42.

116. (Once Amended) An isolated polynucleotide complementary to the polynucleotide of claim 36, wherein said polynucleotide is not Genbank Accession No. X91553.

124. (Once Amended) An isolated polynucleotide complementary over its full length to the polynucleotide of claim 37.

140. (Once Amended) An isolated polynucleotide comprising a nucleic acid encoding a fragment of SEQ ID NO:2 or a fragment of a protein encoded by the cDNA contained in ATCC Deposit No. 209691 or 209641, wherein said fragment [modulates] inhibits or enhances the differentiation and/or proliferation of immune cells.

151. (Once Amended) The isolated polynucleotide of claim 37 wherein said encoded polypeptide [modulates] inhibits or enhances the proliferation and/or differentiation of immune cell.

Please add the following new claims:

152. (New) The isolated polynucleotide of claim 140, wherein said fragment inhibits the differentiation and/or proliferation of immune cells.

153. (New) The isolated polynucleotide of claim 140, wherein said fragment enhances the differentiation and/or proliferation of immune cells.

154. (New) The isolated polynucleotide of claim 151 wherein said encoded polypeptide inhibits the proliferation and/or differentiation of immune cell.

155. (New) The isolated polynucleotide of claim 151 wherein said encoded polypeptide enhances the proliferation and/or differentiation of immune cell.